

REMARKS

Claims 1-5, 7-11, 13-15, and 17-32 are pending. Claims 6, 12 and 33-38 are canceled. No amendments to the claims have been made in this response.

Rejection under 35 USC §102

Claims 1-5, 7-9, 11, 13, 19, 22, 24, 26, 28, 30 and 31 were rejected under 35 USC §102(a) over Cho. The Office Action indicated that an English copy of the priority document would overcome this rejection. Applicants enclose herewith an English translation of the priority document. Accordingly, Applicants submit that this rejection has been overcome and notice to this effect is respectfully requested.

Rejections under 35 USC §103

Claims 1-5, 7-9, 11, 13, 17-19, 21, 22, 24, 26, 28, 30 and 31 were rejected under 35 USC §103(a) over Mandell in view of Wilson. Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP §2143.

Mandell describes retroviral vectors containing DNA that encodes rat iodine transporter (Na^+/I^-) NIS gene. Wilson et al describes replication defective adenovirus (AV) encoding VLDL receptor gene. Wilson et al proposes expression of the adenovirus vector in hepatic cells and for treatment of metabolic disorders. The Examiner states that it would be obvious for one skilled in the art to use the adenoviral vector described in Wilson et al to express NIS gene in place of the retroviral vector described in Mandell.

Applicants respectfully submit that Mandell cannot properly be combined with Wilson. The skilled artisan is aware that the mechanism of replication for retrovirus and adenovirus are different and not interchangeable. Most notably, retroviruses integrate into the genome of the host cells. Thus, retroviral vectors harbouring a transgene will also integrate into the host genome and, in turn, the transgene is transmitted to the progeny of dividing cells undiluted. On the contrary, adenoviruses do not integrate into the host cell's genome; rather they replicate as episomal elements in the nucleus

of the host cell. Thus, it is expected that a population of host cells transduced with an adenoviral vector containing a transgene will be diluted in the progeny of actively dividing cells. This dilution would be expected to be more acute when the host cells are cancer cells undergoing uncontrolled division. Accordingly, adenoviral vectors cannot be considered equivalent to retroviral vectors and used interchangeably.

One skilled in the art faced with the technical problem of treating a whole population of actively dividing cells would have not considered using an adenoviral vector to more efficiently pass on a transgene of interest to its cell progeny. Accordingly, the skilled artisan would not have substituted the adenovirus taught in Wilson for the retrovirus taught in Mandell because there was no expectation of success. It is impermissible to combine the references in hindsight to achieve Applicants' invention.

Applicants unexpectedly found the efficacy of expression of NIS in cancerous cells when said cells are treated with adenovirus harboring the NIS gene. According to Mandell, A375 tumor cells infected with retroviruses encoding NIS gene accumulate more radionucleotide *in vivo* than non-infected tumor cells. The relative uptake of ¹²³Iodine was ~7 fold greater than for non-transduced tumor cells (see page 664, right hand column, lines 8-9. According to the present invention, the level of ¹²⁵Iodine uptake is ~10 fold greater in tumor cells infected with adenoviral vectors encoding NIS compared to control tumor cells (see Table in Example 4). The adenoviral vectors encoding NIS of the claimed invention unexpectedly display increased efficacy of radiolabeled iodine accumulation in the tumor cell compared to tumor cells transfected with retroviral vectors encoding NIS as disclosed by Mandel et al.

Applicants submit that because there is no expectation of success from the combination of references cited above and because there is no motivation or suggestion to combine these references, a *prima facie* case of obviousness has not been properly established. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim 10 was rejected under 35 USC §103(a) over Mandell and Wilson, as above, in further view of Sauvage. Applicants respectfully traverse this rejection. Deficiencies of the first two references to establish a *prima facie* case of obviousness are noted above. Sauvage does not remedy these deficiencies. Accordingly, claim 10 is patentable over the applied art for at least the same reasons that claim 1 from which it ultimately depends is patentable over the applied art. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 14, 20, 23, 25, 27, 29 and 32 were rejected under 35 USC §103(a) over Mandell in view of Wilson, in further view of Hidaka. Applicants respectfully traverse this rejection. Deficiencies inherent in combining Mandell and Wilson are discussed above. Hidaka does not remedy the aforementioned deficiencies. Accordingly, claims 14, 20, 23, 25, 27, 29 and 32 are patentable over the applied art for at least these same reasons that claim 1 from which they ultimately depend is patentable over the applied art. Reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all pending rejections. Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,



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